

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P02/065-bzgs	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 03/04063	International filing date (day/month/year) 17/04/2003	(Earliest) Priority Date (day/month/year) 18/04/2002
Applicant MERCK PATENT GMBH		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/04063

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/755 C07K7/08 A61K38/37 A61K38/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 03195 A (CHIRON CORP ; INNIS MICHAEL (US); COHEN FRED E (US); HUNG DAVID T () 30 January 1997 (1997-01-30) page 22, line 6 - line 9; claim 36 ---	1-5,8-11
X	WO 00 34317 A (ADAIR FIONA SUZANNE ; CARR FRANCIS JOSEPH (GB); HAMILTON ANITA ANNE) 15 June 2000 (2000-06-15) page 3, line 13 -page 5, line 18 page 8, line 12 - line 13 ---	1-5,9-16
Y	WO 98 52976 A (BIOVATION LTD ; CARR FRANCIS J (GB)) 26 November 1998 (1998-11-26) page 3, line 5 -page 4, line 21 ---	1-5,9-16
Y	WO 99 53038 A (GENENCOR INT) 21 October 1999 (1999-10-21) page 4, line 6 -page 6, line 25; example 1 ---	1-5,9-16
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

26 August 2003

Date of mailing of the international search report

04/09/2003

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/04063

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 59244 A (BROOKS TONY ;ECLAGEN LTD (GB); KEMP GRAHAM (GB); CARR FRANK (GB);) 30 December 1998 (1998-12-30) page 3, line 27 -page 5, line 37 page 9, line 16 - line 25 ----	1-5,9-16
Y	ALTUVIA Y ET AL: "RANKING POTENTIAL BINDING PEPTIDES TO MHC MOLECULES BY A COMPUTATIONAL THREADING APPROACH" JOURNAL OF MOLECULAR BIOLOGY, LONDON, GB, vol. 249, no. 1, 1995, pages 244-250, XP000925520 ISSN: 0022-2836 the whole document ----	1-5,9-16
Y	MEISTER G E ET AL: "Two novel T cell epitope prediction algorithms based on MHC-binding motifs;comparison of predicted and published epitopes from Mycobacterium tuberculosis and HIV protein sequences" VACCINE, BUTTERWORTH SCIENTIFIC, GUILDFORD, GB, vol. 13, no. 6, 1 April 1995 (1995-04-01), pages 581-591, XP004057605 ISSN: 0264-410X the whole document ----	1-5,9-16
Y	BRUSIC VLADIMIR ET AL: "MHCPEP, a database of MHC-binding peptides: Update 1997" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 26, no. 1, 1 January 1998 (1998-01-01), pages 368-371, XP002204283 ISSN: 0305-1048 the whole document ----	1-5,9-16
Y	WO 99 46274 A (UNIV EMORY) 16 September 1999 (1999-09-16) the whole document ----	1-5,9-16
P,X	WO 02 096454 A (COLLEN RES FOUNDATION VZW D ;SAINT-REMY JEAN-MARIE R (BE); JACQUEM) 5 December 2002 (2002-12-05) claims 20,27,30,42; figures 2,3,5 ----	1-5,9-16
P,X	WO 02 090542 A (DI GIAMBATTISTA MARIO ;LAUB RUTH (BE); DEPT CENTRAL DE FRACTIONNEM) 14 November 2002 (2002-11-14) the whole document -----	1-5,9-16

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 6 and partially claims 1-5, 9-16

A modified human factor VIII molecule, the modification being a substitution in peptide P10 according to Table 2 (at positions 1208, 1209 or 1210), the encoding DNA sequence, a pharmaceutical composition comprising said modified factor, the peptide molecule P10 or a substituted form thereof and their use in a vaccine or for manufacturing a modified factor VIII molecule.

2. Claims: 7 and partially claims 1-5, 9-16

A modified human factor VIII molecule, the modification being a substitution in peptide P8 according to Table 2 (at positions 1011 or 1013), the encoding DNA sequence, a pharmaceutical composition comprising said modified factor, the peptide molecule P8 or a substituted form thereof and their use in a vaccine or for manufacturing a modified factor VIII molecule.

3. Claims: 8 and partially claims 1-5, 9-16

A modified human factor VIII molecule, the modification being a substitution in peptide P7 according to Table 2 (at position 823), the encoding DNA sequence, a pharmaceutical composition comprising said modified factor, the peptide molecule P7 or a substituted form thereof and their use in a vaccine or for manufacturing a modified factor VIII molecule.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: partially 1-5,9-11,13-15

Present claims 1-5, 9-11 and 13-15 relate to an extremely large number of modified factor VIII molecules, which are defined by reference to a desirable characteristic, namely being non- or less immunogenic than wild type factor VIII by reduction of elimination of one or more T-cell epitopes which bind to MHC class II molecules.

Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds as defined in claims 6-8.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/04063

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: partially 1-5, 9-11, 13-15
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/04063

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9703195	A	30-01-1997	AU 6486196 A WO 9703195 A1	10-02-1997 30-01-1997
WO 0034317	A	15-06-2000	AU 1667600 A CA 2342967 A1 CN 1294596 T EP 1051432 A2 WO 0034317 A2 JP 2002534959 T AU 4635699 A	26-06-2000 15-06-2000 09-05-2001 15-11-2000 15-06-2000 22-10-2002 24-01-2000
WO 9852976	A	26-11-1998	AU 736549 B2 AU 7539398 A EP 0983303 A1 WO 9852976 A1 GB 2339430 A JP 2002512624 T US 2003153043 A1	02-08-2001 11-12-1998 08-03-2000 26-11-1998 26-01-2000 23-04-2002 14-08-2003
WO 9953038	A	21-10-1999	AU 752934 B2 AU 3645499 A BR 9909640 A CA 2327311 A1 CN 1297484 T CZ 20003789 A3 EP 1073754 A2 JP 2002511251 T NO 20005153 A PL 343509 A1 WO 9953038 A2 US 6596525 B1 US 6218165 B1	03-10-2002 01-11-1999 19-12-2000 21-10-1999 30-05-2001 15-08-2001 07-02-2001 16-04-2002 11-12-2000 27-08-2001 21-10-1999 22-07-2003 17-04-2001
WO 9859244	A	30-12-1998	AU 8118398 A WO 9859244 A1	04-01-1999 30-12-1998
WO 9946274	A	16-09-1999	US 6180371 B1 AU 747644 B2 AU 2995699 A CA 2322508 A1 CN 1297452 T EP 1062224 A1 HU 0101317 A2 JP 2002506076 T NO 20004497 A NZ 506771 A PL 342887 A1 WO 9946274 A1 US 2003068785 A1 US 6458563 B1	30-01-2001 16-05-2002 27-09-1999 16-09-1999 30-05-2001 27-12-2000 28-08-2001 26-02-2002 07-11-2000 26-11-2002 16-07-2001 16-09-1999 10-04-2003 01-10-2002
WO 02096454	A	05-12-2002	WO 02096454 A1 WO 02098454 A2	05-12-2002 12-12-2002
WO 02090542	A	14-11-2002	US 2002068303 A1 WO 02090542 A2	06-06-2002 14-11-2002

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